REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

I. Claim Amendments

By the foregoing amendments to the claims, claims 21, 29, 32, 34, and 35 have been amended, and new claims 38-40 have been added. Support for these amendments can be found throughout the application as filed.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

II. Restriction and Election of Species Requirements

The Examiner has acknowledged Applicants' elections with respect to the restriction and election of species requirements. Further, given Applicants' election of expression vectors, the Examiner has requested that claim 29 be amended so as to be directed to the expression vectors.

In response, claim 29 has been amended accordingly.

III. Foreign Priority

The Examiner has acknowledged Applicants' claim for foreign priority. However, the Examiner has indicated that the certified copy of the French priority application has not been filed.

In response, Applicants submit herewith the following documents: a certified copy of the French priority document (FRANCE 03/06772, filed June 5, 2003); an English language translation of the French priority document; and a Declaration stating that the translation of the certified copy is accurate.

IV. Response to Claim Rejections Under 35 U.S.C. § 112

The Examiner has rejected claims 21 and 34 with respect to recitation of "means necessary to the expression." It is unclear from the Examiner's rejection whether such rejection is made under 35 U.S.C. § 112, second paragraph or sixth paragraph.

Irrespective, contrary to the Examiner's assertion on page 3, paragraphs 8-9, of the Office Action, Applicants submit that the application does define the "means" on page 9, lines 10-25, of the translation. In particular, the application defines the "means" as any means that make it possible to obtain the encoded polyprotein and polypeptide, including a promoter and a transcription terminator.

However, to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, claim 21 has been amended to recite that the polyprotein and the polypeptide are "placed under the regulatory elements necessary to [their] expression."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

V. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 29 and 37 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly lacking enablement.

Specifically, the Examiner has acknowledged that the specification enables using an expression vector encoding an HCV antigenic polyprotein or polypeptide to induce an immune response. However, the Examiner has further stated that the specification does not enable using the expression vector to prevent HCV infection.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended by canceling the term "prevention."

Applicants submit that the present specification fully enables the subject matter of the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the enablement rejection.

VI. Response to Claim Rejections Under 35 U.S.C. § 102

A. Claims 21, 23, 26, 28, 29, 35 and 36 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Pancholi et al. (Jan 2003, J. Virol. 77: 382-390). This

rejection is respectfully traversed.

The present inventors have surprisingly found that an expression vector expressing a nucleotide sequence encoding HCV polyprotein NS3/NS4 and a nucleotide sequence encoding HCV polypeptide NS5b is sufficient to inhibit or control HCV infection and to induce an immune response in an animal infected by HCV. Accordingly, the present claims recite such expression vectors and methods for using the same.

In contrast to the present claims, Pancholi et al. describe a method of immunization following vaccination with DNA and/or canarypox vectors encoding all HCV proteins in the form of 2 polycistronic constructs. The reference vectors were constructed by inserting HCV genomic portions, the first portion referred to as C-NS3 construct extending from the capsid through the NS3 genes, and the second portion referred to as NS3-NS5 construct extending from the NS3 through the NS5 genes (see "Material and Methods," page 383, top of the second column). As a result, the polypeptide encoded by the C-NS3 construct is a single chain polypeptide encompassing 5 fused HCV proteins (Core, El and E2 envelopes, NS2 and NS3), and the polypeptide encoded by the NS3-NS5 construct is a single chain polypeptide encompassing the HCV NS3, NS4, NS5a and NS5b proteins.

However, in contrast to the present invention, Pancholi et al. does not teach or even suggest expression vectors and methods that do not express the HCV NS5a gene and otherwise have the features of the present invention (*i.e.* expression of NS3 and N54 in a single chain polypeptide (NS3/NS4 polyprotein) and NS5b independently).

Therefore the present claims are novel over the teachings of Pancholi et al., and Applicants respectfully request reconsideration and withdrawal of this rejection.

B. Claims 21, 23, 26, 28, 29 and 35 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Coil et al. (US 6,986,892). This rejection is respectfully traversed.

US 6,986,892 discloses an expression vector into which is inserted the HCV genomic portion encoding amino acids 1242-3011 and a method for using such a construct to provide an anti-HCV immune response. The reference expression vector encodes a single chain polypeptide encompassing the HCV NS3, NS4, NS5a and NS5b proteins.

However, US 6,986,892 does not teach or even suggest the subject matter recited in the present claims. In particular, the reference does not teach or suggest vectors and methods

that do not express the HCV NS5a gene, and that have been designed to express NS3 and NS4 as a single chain polypeptide (NS3/NS4 polyprotein) and NS5b independently.

Therefore the present claims are novel over the teachings of US 6,986,892, and Applicants respectfully request reconsideration and withdrawal of this rejection.

C. Claims 21-23 and 28-29 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Paliard et al. (W001/30812). This rejection is respectfully traversed.

W001/30812 discloses a method for providing an anti-HCV immune response using HCV NS3, NS4 and NS5a proteins or HCV NS3, NS4, NS5a and NS5b polypeptides expressed from expression vectors as a single chain polypeptide or as individual polypeptides (*see, e.g.*, page 18, 1ines 16-23 of the reference). In contrast to the present invention, which excludes the expression and use of NS5a, the compositions, expression vectors and methods disclosed in W001/30812 require the presence of NS5a . Moreover, W001/30812 fails to teach or even suggest expression of the NS3 and NS4 polypeptides as a single- chain polyprotein and NSSb as an individual polypeptide.

Therefore, the pending claims are novel over W001/30812, and Applicants respectfully request reconsideration and withdrawal of this rejection.

D. Claims 21-23, 28 and 29 have been rejected under 35 U.S.C. § 102(e) as purportedly being anticipated by Paliard et al. (US 7,285,539 or US 6,562,346).

US 6,562,346 and US 7,285,539 teach methods and compositions relying on HCV NS3, NS4, and NS5a proteins or alternatively HCV NS3, NS4, NS5a and NS5b proteins.

As the pending claims exclude the presence of NS5a, they are novel over Paliard patents US 6,562,346 and US 7,285,539. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

E. Claims 21, 23, 28 and 36 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by Houghton et al. (US 6,312,889).

US 6,312,889 teaches methods and compositions relying on combinations of HCV polypeptides that include Core and at least one additional HCV polypeptide (NS3, NS4, and/or NS5).

Since the pending claims exclude the presence of HCV Core polypeptides, the claims are novel over the US 6,312,889 Houghton et al. patent. Accordingly, Applicants

respectfully request reconsideration and withdrawal of this rejection.

VII. Response to Claim Rejections Under 35 U.S.C. § 103

A. Claims 26-27, 32 and 34-37 have been rejected under 35 USC 103(a) as purportedly being unpatentable over Paliard et al. (W001/30812). These claims have also been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Paliard et al. (US 7,285,539 or US 6,562,346). These rejections are respectfully traversed.

As discussed above in response to the outstanding § 102 rejections, the compositions, vectors and methods disclosed in the Paliard et al. references rely on HCV NS3, NS4, and NS5a or alternatively HCV NS3, NS4, NS5a and NS5b expressed as a single chain polypeptide (fused together as in the HCV genome) or as individual polypeptides.

The presence of NS5a is essential to Paliard's compositions, vectors and methods, particularly as two epitopes were identified in NS5a that activate the HCV-specific T cell response (*see* page 15, lines 22-25 of W001/30812; column 10, lines 35-40 of US 6,562,346; and column 10, lines 41-49 of US 7,285,539). Applicants emphasize that these epitopes are present respectively at positions 2152-2160 (HEYPVGSOL; SEO ID NO: 1) and at positions 2224-2238 (AELIEANLLWRQEMG; SEQ ID NO: 2), in other words within NS5a.

Therefore, a person of ordinary skill in the art would have expected that NS5a was necessary to provide effective anti-HCV immunity. Accordingly, the skilled person would not have been motivated to exclude NS5a, as in the present expression vectors, and would not have had a reasonable expectation of success.

Because the Paliard et al. references, taken individually or in combination, do not teach or suggest the subject matter of the present claims, Applicants respectfully request reconsideration and withdrawal of these rejections.

B. Claims 21, 23, 28 and 36 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Houghton et al. (US 6,312,889) in light of Clark (1997, J. Gen. Virol. 78:2397 -2410). This rejection is respectfully traversed.

As discussed above, US 6,312,889 teaches combinations of HCV polypeptides that include Core and additional HCV polypeptide(s) selected from NS3, NS4, and/or NS5. The combination can be in the form of a single chain polypeptide (a fusion polypeptide) or in the form of a mixture of individual polypeptides. Combinations encompassing Core, NS3, NS4

and NSS are exemplified (C. NS3. NS5 and NS3/NS4/NS5/C; column 5, lines 4-11). As disclosed at column 4, lines 46-47 and in Example 5 of the '889 patent, a preferred NS5 antigen comprises amino acids 2054-2464 (by reference to Figure 1). Applicants note that the portion of the HCV genome spanning amino acids 2054-2464 includes the vast majority of NS5a (366 residues) and only a very short portion of NS5b (44 residues). (This is evidenced by Clark in view of the HCV genomic organization illustrated in Figure 1, which clearly shows the position of the NS5a and NS5b regions, located respectively between amino acid positions 1973 to 2420 and 2421 to 3011.) Thus, the preferred combinations of HCV polypeptides disclosed by Houghton et al. comprise a large portion of NS5a as well as Core.

Thus, the state of the art at the time of filing would have taught the skilled person to include NS5a (as taught by Paliard et al. and Houghton et al.) and Core (as taught by Houghton et al.) in order to provide an effective anti-HCV immune response.

In this regard, Applicants draw the Examiner's attention to Example 3.3 of the present invention (at pages 31-34 of the specification) which illustrates immunity induced in a mouse model by adenovirus vectors expressing different combinations of HCV polypeptides. As apparent from Table 1, the combinations including either NS5a (Ad NS3/NS4 + NS5b + NS5a) or Core (Ad NS3/NS4 + AdNS5b + AdCE1E2) are less effective to immunize mice against HCV than the expression vector of the present invention (AdNS31NS4 + NS5b). This is an unexpected result that is not disclosed, taught or suggested in the cited references either alone or in combination.

In light of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

This response is made without prejudice or disclaimer to any non-elected subject matter, and Applicants reserve the right to file one or more continuation and/or divisional applications directed to any non-elected subject matter.

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions related to this response, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney at the below-listed telephone number concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: April 24, 2008

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